G.N.Ramachandran

A Jewel in the Crown of Modern Indian Science

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Vigyan Prasar

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Foreword

The year 2004 marks the fifty years of the "Madras Triple Helix", the molecular model proposed for the fibrous protein collagen by Professor Gopalasamudram Narayana Ramachandran (08 October, 1922 - 07 April 2001), physicist turned outstanding structural biologist, and his group.

Though collagen is a relatively simple protein, its structure remained a mystery till 1954. Incidentally, this was just a year after the double helical structure for DNA by Watson and Crick was propounded. Ramachandran thus joined the big league of structural biologists when he was hardly 32. Ramachandran went on to enunciate the fundamental stereochemical principles for conformational analysis of proteins through the famous Ramachandran plot.

This booklet by Dr. Subodh Mahanti briefly describes the life and work of this great Indian Scientist.

V. B. Kamble
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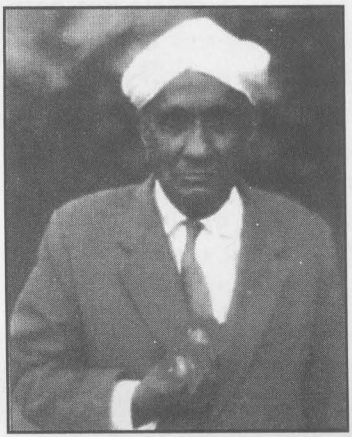
most brilliant Indian scientists of the 20th century. He made several important discoveries in molecular biophysics, especially in the study of protein structure. The discovery of triple helical structure of collagen was a fundamental advance in the understanding of peptide structure. "The Ramachandran phi-psi plot" or simply the "Ramachandran Plot" has become a standard description of protein structures in text books.

When Ramachandran was doing research in biophysics in India the subject was just taking shape in the advanced countries and undoubtedly he was a pioneer in this field. He started two centres of molecular biophysics, first at the University of Madras, Chennai and second at the Indian Institute of Science, Bangalore. Both the centres became internationally recognised centres for research in biophysics. Ramachandran inspired a large number of young people to take up science, who made significant contribution in various aspects of biophysics. Ramachandran had a deep interest in philosophy and in classical Indian and western music. He interpreted the philosophical ideas of Syaad Nyaan, 'the doctrine of may be', an age-old system in Jain philosophy, in mathematical form which he called 'Boolean Vector Matrix Formulation'.



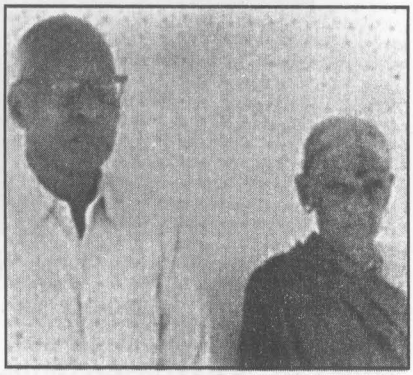
Prof. C.V. Raman

Besides being an accomplished great scientist he was a very good speaker. He could easily present highly complicated concepts in simple words which could be understood even by high school students. These days

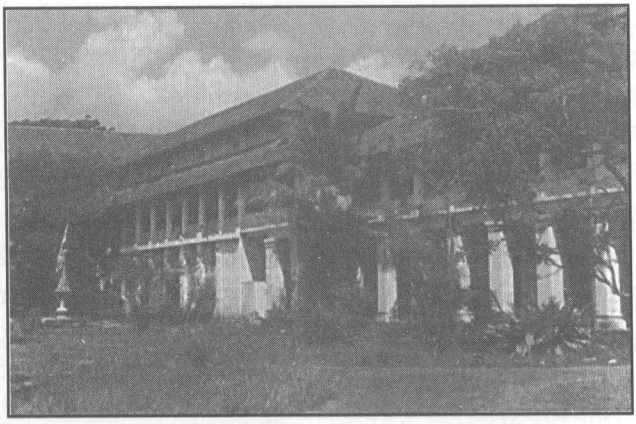
we hardly find such a scientist particularly in India. By any standards he was a superb teacher. He wrote poems on science, religion, philosophy and the Upanishads. He made exemplary donations to charitable institutions.

Early years and Education

Ramachandran was born on October 8,1922 in Ernakulam near Cochin in Kerala. Ramachandran was the eldest son of G.R. Narayana Iyer and Lakshmi Ammal. At the time of his birth, Cochin was ruled by a Maharajah, who had full autonomy under the British Government. The Maharajah of Cochin was an enlightened ruler, under whose aegis educational and cultural institutes thrived. For higher education Cochin had a college known as the Maharajah's College. His father was a well-known professor of mathematics and he retired as the Principal of Maharajah's College. To quote Ramachandran on his father : "Because of his ability and thoroughness he became the most senior and respected member of the department and retired as the Principal. He had a very sharp mind in mathematics and he used to teach me mathematics. I had been exposed to most of the theories in analytical geometry even before I went to college. When I was in high school, he would bring books on mathematics from the library and give me some challenging theorem to prove every day. He would write equations and ask me to solve them. He was a wizard in mathematics". So it was no wonder



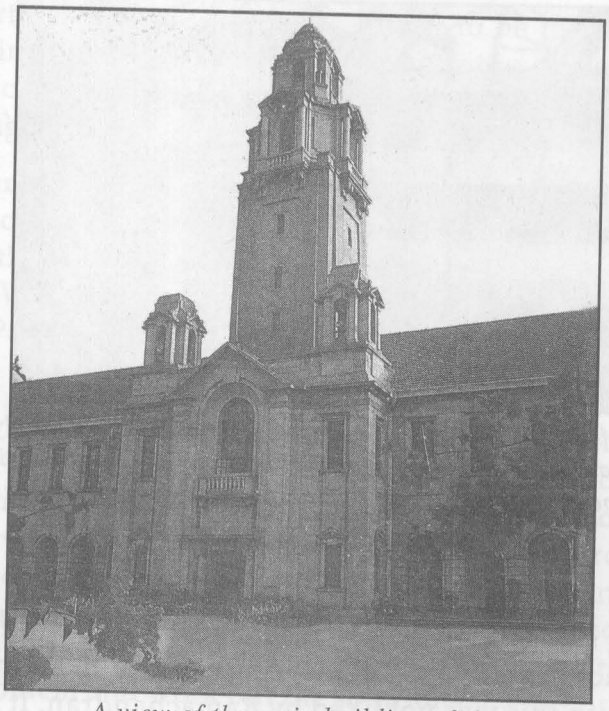
Ramachandran's parents, Professor G.R. Narayana Iyer and Srimathy Laxmi Ammal



Maharaja's College, Ernakulam,
where Ramachandran had his early college education.

that Ramachandran would develop a deep interest in mathematics since his childhood. We are told that as a school student he used to get a perfect score of 100 on all his mathematics examinations.

Ramachandran had his early schooling in a government school in Ernakulum. After the Intermediate Examination, in which he stood first in the entire Madras State, Ramachandran joined the St. Joseph's College in Trichy in 1939. Here he enrolled himself in the BSc (Honours) degree in physics. Ramachandran's decision to study physics instead of mathematics in which he always got a perfect score of 100 was largely influenced by his father. To quote his biographer and student Raghupathy Sarma: "Ramachandran, with his extensive interest and knowledge, could have easily studied for the honours degree in mathematics. He rightly felt that Ramachandran already knew so much mathematics that if he did join the honours programme, his college teachers would have "nothing new" to teach him. Therefore, he advised Ramachandran to join Physics



A view of the main building of the Indian Institute of Science, Bangalore

honours and ask for special permission to study chemistry in place of mathematics as the subsidiary subject. Ramachandran always felt that this was a very wise choice on his part, as this introduction to chemistry helped him substantially in his later research. Among the teachers in St. Joseph's College who stimulated Ramachandran's interest in physics were P.E. Subramaniam and a Jesuit priest, Father Rajam. Ramachandran stood first among all the physics honours students in the entire Madras Presidency.

Joining Indian Institute of Science

Ramachandran's father, Narayana Iyer, wanted his son to take up the Indian Civil Service Examination. However, Narayana Iyer failed to persuade his son in

Alagappa Chettiar College of Technology in Guindy, Madras where the research laboratories of the Physics Department headed by Ramachandran were also located.

doing so. He then sent Ramachandran to Delhi to take the Indian Railway Engineering Service Examination. But even this was not liked by Ramachandran. It is said that he deliberately performed poorly in the entrance examination to ensure that he was not selected. After this digression Ramachandran joined the Electrical Engineering Department of the Indian Institute of Science, Bangalore, for his MSc degree. However, soon he realised that his interests lay in physics and so he decided to switch over to it. It is very likely that his decision might have been influenced by the fact that at that time the legendary Prof. C.V. Raman was the Director of the Institute as well as the Head of the Department of Physics. Knowing Ramachandran's interest, Prof. Raman requested the head of the Electrical Engineering Department to allow Ramachandran to join the Physics Department. However, when the request was persistently refused, Raman told the Head of the Electrical Engineering Department: "I am admitting Ramachandran into my

department as he is a bit too bright to be in yours..." And in this way Ramachandran not only came to the physics department but he eventually became the most distinguished of Raman's students.

Raman's influence

Ramachandran was deeply influenced by C.V. Raman. The other two scientists who influenced Ramachandran were William Lawrence Bragg (1890-1978) and Linus Carl Pauling (1901-1994).

To know a little about how he started his research career in the Indian Institute of Science and what he thought about Raman, we quote Ramachandran : "Raman knew that I understood principles of optics. He gave me a very important problem. This problem has been treated earlier by Raleigh- Jeans. Raman gave me Raleigh's paper and a book pertaining to this problem. In one day I was able to write the equation to the problem and work out the solutions. I was horrified to see the solution containing several hyperbolic sines and cosines. I had seen it before and I went to the library and found this volume with several formulas and equations. I was very pleased to find completely corresponding equations and solutions in that book. I wrote a very rigorous proof and showed it to Raman. He was so pleased. He said we should publish the results, this was within one week of my joining Raman. That was a very useful result, which I used twenty years later in studying crystal perfection and the difference between mosaic and perfect crystals."

"Raman recommended me for a scholarship of 60 rupees a month. But the administrators of the Institute said that I had to have a master's degree. Raman said, 'Don't worry about it, I will give you a fellowship of 130 rupees a month, you get an associateship degree from the Institute.' There were no courses to take, only

An auditorium of the Central Leather Research Institute in Madras was Named "Triple Helix", after the triple helical structure of collagen.

research. The degree awarded was called A.I.I.Sc. I was in charge of setting up an X-ray diffraction unit, it was a demountable X-ray tube."

"In the Institute I used to give lectures on crystallography, starting with symmetry. I studied crystallography all by myself. I studied a book on group theory, and it became very useful throughout, particularly in my work on logic. There were very few books on group theory and this book was by Herman Weyl. That changed my whole attitude to science" .

"Raman had great respect for students who were better than him in mathematics. He gave me another problem to study the scattering of light by small particles, 3 or 4 times the wavelength of the radiation used."

"Raman had ten to fifteen students working under him. He was a virtuoso, and each student was working on a different problem. Raman tried to bring famous scientists from abroad and he even tried to get a faculty

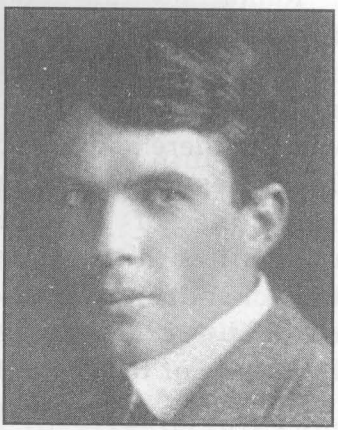
position for Max Born, who was a visiting professor in his department. He wanted Erwin Schrodinger to come to India. This was a time when many scientists were leaving Germany. At that time Raman was the Director of the Institute, but after the first three years, the administrators of the Institute told him: 'We don't want you."

Ramachandran obtained his MSc degree in 1944 from the Madras University. In those days the Indian Institute of Science was not a degree granting institution. Students working there had to submit their theses for a degree from one of the other universities in the country. Ramachandran's thesis for his MSc degree contained the results of the theoretical and experimental investigations that he carried out on the propagation of light through optically heterogeneous media. The external examiner of his thesis was Prof. K.S. Krishnan, who was then Professor of Physics at the University of Allahabad. After obtaining his master degree Ramachandran continued his research work for a doctoral degree under the supervision of Prof. Raman. His doctoral research involved photo-elasticity and thermo-optic behavior of different solids such as diamond, fused quartz, fluorspar and zinc blende. Research publications resulting from his doctoral work contained some of the earliest applications of X- ray diffractions to the study of variation in perfection of

Prof. K.S. Krishnan

crystals. He also coined the term 'topograph' for such pictures. It should be emphasised that the research paper published carried his name as the single author and did not include Raman's name. These days hardly any research scholar, particularly in India, will be allowed to do the same.

From Bangalore to Cambridge



William Lawrence Bragg

Ramachandran obtained his Doctor of Science (DSc) degree in 1947 and decided to go to Cambridge in England to work in the Cavendish Laboratory, where Sir William Lawrence Bragg was the Director. Ramachandran succeeded in getting a prestigious scholarship for higher studies in England provided by the Royal Commissioners of the 1851 Exhibition. As he had already studied X-ray diffraction for his doctoral work in the Indian Institute of Science he easily became a part of the Cavendish group of crystallographers. However, he could not get the opportunity to work directly under Lawrence Bragg. He was assigned to work with Dr. W. A. Wooster.

In Cambridge, Ramachandran decided to work again for a doctoral degree. While explaining why he chose to work for a second doctoral degree in Cambridge, Ramachandran said : "In 1947 I went to Cambridge, England, to work in the Cavendish Laboratory with Dr. Wooster. Dr. Taylor was the head of the crystallography group. I did not attach myself to any College in Cambridge and I was in Fritzwilliam

House. I did not like to wear those gowns like the ones the undergraduates were expected to do. I decided to work for a doctoral degree because then there would be something to show for my work; simply getting a few publications does not impress authorities in India. My decision may have definitely helped me in getting my first job in Madras..." Ramachandran considered his stay in Cambridge quite fruitful. He said : "Going and staying for two years in Cambridge did a lot of good things for my research. I attended Dirac's Course on Principles of Quantum Mechanics...Most students, in Dirac's class were undergraduates who were second-or-third year physics majors. He used matrices and tensors a lot. Later I used the same symbols in my mathematical treatment of logic. Whatever I tried to design for my experiments could not easily be implemented because there was no suitable engineering programme in Cambridge University." In Cambridge, Ramachandran worked in three projects — instrumentation, electronics and the development of a mathematical theory to study diffuse X-ray diffraction, and use it in determining the elastic constants of crystals.

Admiration for Pauling

In Cambridge he also met Linus Pauling for the first time. This was a great moment for young Ramachandran, at the time he was 25 years old. For Ramachandran, Pauling was a great hero, who had just discovered the alpha helical structure of polypeptides. Moreover Ramachandran's vision of chemistry was shaped by reading Pauling's books and articles. Ramachandran admired Pauling throughout his life. He even dedicated a poem to Pauling. Ramachandran wrote a number of poems on scientific concepts. We

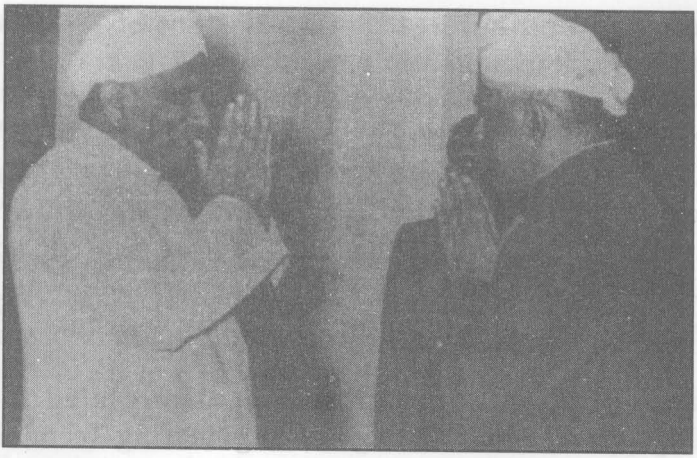
quote below two stanzas from the poem that he dedicated to Pauling.

Linus Pauling
Is a name to conjure with,
In chemical bonding
And whatever forthwith
Follows for all matter,
Both inanimate and alive
Their nature and character
And how they will behave.
His great alpha helix,
That opened the path
For the solution of structures
Of all biopolymers,
Is a star that will adorn
The firmament of Science,
For it has revealed to biologists
Completely new ways.

Linus Pauling

Return to India

After finishing his doctoral work in Cambridge he returned to India in June of 1949. He was appointed as Assistant Professor of Physics, in the Department of Physics of the Indian Institute of Science. He was made in charge of the X-ray Diffraction Laboratory that he was instrumental in building as a student. Earlier in the same department he had worked for his DSc degree under the supervision of Prof. C.V. Raman. But this time Raman was not there. He had left the Institute of Science and had started his own institute, Raman Research Institute. The Department of Physics was then headed by Prof. R.S. Krishnan. Ramachandran could attract some very bright young men such C. Radhakrishnan, Gopinath Kartha and Y.T. Thatachary to his research group. The X-ray Diffraction Laboratory



C.V. Raman & A.L. Mudaliar

set up by Ramachandran grew over the years to home one of the strongest research groups in the physics department.

Shifted to Madras University

After about two years in the Indian Institute of Science he shifted to Madras University, one of the three universities that were first set up in India. The other two were Calcutta University and Bombay University. At that time Dr. A. Lakshmanaswamy Mudaliar was the Vice Chancellor of the Madras University. It was Mudaliar, who being influenced by the legendary. Prof. C.V. Raman, planned to establish post-graduate department in experimental physics at the University of Madras. He requested Prof. Raman to head this newly established department and he offered him financial and administrative autonomy for the development of the proposed department. Raman expressed his inability to head the department; but at the same time he recommended the name of Ramachandran. And this is how Ramachandran joined the Madras University in October of 1952 as the first

professor and head of the Department of Physics. At the time, Ramachandran was just 30 years old. The Department of Physics was started with two faculty members, Ramachandran in experimental physics and Alladi Ramakrishnan in theoretical physics. Ramakrishnan was the first to join the department in April, 1952 and in that way he was the founding member of the department. The department was first located in a single room of the main building of the University on the Marina beach in Madras. Ramachandran's laboratory was also located in the Alagappa Chettiar College of Engineering Technology Complex in Guindy, a suburb of Madras.

Ramachandran's research work carried out at the Madras University brought an unprecedented level of recognition to the University. He organised two international conference in 1963 and 1968 and he was successful in bringing some of the most famous scientists in molecular biology and biophysics to Madras viz. Linus Pauling, Severe Ochoa, Mauris Wilkins, Paul Flory and others.

Left Madras University

After the retirement of Mudaliar as Vice Chancellor of the Madras University, it became extremely difficult for Ramachandran to carry out his research work. Mudaliar was succeeded by Sundaravadivelu, who was the Director of Public Education in the State Education Department. It has been reported that Sundaravadivelu had no appreciation for Ramachandran's seminal research contribution and instead of supporting Ramachandran's efforts he created obstacles wherever he could. And so finally Ramachandran resigned from the Madras University in 1970 and came back to the Indian Institute of Science where he had earlier studied and worked for two years after coming back from

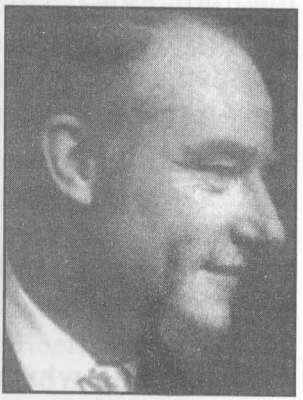
Cambridge. At the time Professor Satish Dhawan, a well-known space scientist, was the Director of the institute. Ramachandran was given the responsibility of starting a new department of molecular biophysics. The department which was formally started in 1971 grew into a major centre of structural biology.

Research Contributions

To grasp exactly what Ramachandran did, one should have a certain background in physics and chemistry. Here we do not intend to go into detail about his research work.

Explaining why he was attracted to biomolecular conformation he wrote : "I should perhaps explain why I was attracted to this fascinating subject. This is not merely a personal history, but it has relevance to the reason why researchers in the field of biomolecules turned in the way they did from about the beginning of the 50's. Even in the first year of my pre-doctoral studies in the early 40's with Raman, I was attracted by two books on his shelf, namely "Nature of the Chemical Bond" by Linus Pauling and "Natural and Synthetic High Polymers" by Kurt Meyer. These left a profound impression on me, although at that time I was working mostly on optics and diffraction theory under Prof. Raman. I took crystal chemistry as an extracurricular subject of study and as part of this, crystal structures came in serious consideration. Even at that time, I used to wonder why so few of the materials that formed the building blocks of living systems were fully explored by crystallographic techniques. No doubt, the structures of silk and of cellulose and related materials were reasonably well established, by studies starting right from the 1920s, and finally confirmed by the work of Meyer and his co-workers. Similarly the pioneering studies made by

Astbury on Keratin, myosin, etc., had clarified the fact that there exist two types of structures in the fibrous proteins, namely the alpha and beta types."



F.H.C. Crick

Ramachandran worked in a number of fields in physics, chemistry and biology. He contributed more than 250 publications and several reviews in well-known international journals. His first major research contribution was the discovery of the triple helical structure of collagen. Ramachandran was drawn to collagen by J.D. Bernal's remarks that structural proposals for collagen were unsatisfactory. Bernal made these remarks in a casual conversation during his visit to Madras in 1952. Triple helical structure of collagen was first published in 1955. Ramachandran co-authored this paper with Gopinath Kartha. Their concept of coiled-coil structure proved to be a fundamental advance in the understanding of polypeptide structure. Coiled-Coil structure means each of its three polypeptide chains are arranged in the form of a helix, and then the three chains together form a second helix. However, his structure was criticised by none other than Francis H.C. Crick, who alongwith James D. Watson, unraveled the helical structure of D.N.A, the double helix. Crick and Alexander Rich wrote in the November 1955 issue of Nature: "Very recently Ramachandran and Kartha have made an important contribution by proposing a coiled-coil structure of collagen. We believe this idea to be basically correct but the actual structure suggested by them to be wrong. Their structure consists of three

polypeptide chains each having approximately three-fold screw axis. In addition the chains slowly wind around each other to form a coiled-coil, thus reproducing the observed non-integer screw axis. The major helix is right-handed, the minor one left-handed. Each chain is held to its neighbors by two sets of systematic hydrogen bonds. The allowed sequence of residues is -G-R-P-G-R-P- etc., were G implies glycine only, R implies any residue, but usually proline or Hydroxyproline. We believe this structure to be wrong for two reasons :

It is stereochemically unsatisfactory. In particular there is a very short C alpha C alpha contact of 3.3 A° (normally 3.6 to 4 A°) and an extremely short C -0 contact of 2.6 Abnormally 3.2 to 3.5 A°). In addition, hydrogen bond angles are on the outside limit of the values usually found.

It is not compatible with recent work on the amino acid sequence which shows that -gly-pro-hypro- is a common sequence in collagen."

J. D. Bernal

The criticism of unacceptably short interatomic contact in the proposed structure of collagen led Ramachandran to devise a general method for describing stereochemical criterion for polypeptide structure and proteins. Ramachandran and his colleagues, V. Sasisekharan and C.Ramakrishnan laid the foundations for the conforma-tional analysis of polypeptide chains. They introduced a two dimensional map what is today known in biochemical literature as the "Ramachandran phi -psi diagram" or simply "Ramachandran plot", which provide a

rational basis for describing all stereochemically possible structures of polypeptides. They reduced the 'structure space' of protein chains to two-dimensional with dihedral (torsion) angles serving as variables. This had a profound impact on stereo-chemistry and structural biology.

Fourier transforms fascinated Ramachandran. He applied Fourier transforms for developing the theory of Image Reconstruction from shadowgraphs (such as X-Radiographs) using the Convolution Technique. In 1971 Ramachandran alongwith A.V. Lakshminarayana published a seminal research paper on three-dimensional image reconstruction. This marked the beginning of studies on tomographic methods. The idea was adopted for the development of Catscan equipment which has played an important role in the development of medical diagnosis and surgery. In 1976 Ramachandran turned his attention to Fundamental theory and Mathematical philosophy which led to the development of a new Boolean Algebra Vector Matrix Formulation.

Professor and Mrs. Ramachandran

Twenty-seven students completed their Master of Science (MS) or doctorate (PhD) theses under the supervision of Ramachandran. Many of these students have made significant contributions in the field of biophysics. He was a great teacher.

Awards and Honours

Ramachandran had received over a dozen of national and international awards. He was elected a Fellow of the Royal Society of London in 1977. As a part of its Golden Jubilee Celebration, the Indian National Science Academy created five special research professorships and the first one, the Albert Einstein Professorship went to Ramachandran. The Central Leather Research Institute in Chennai has named the building housing its auditorium "Triple Helix' after the triple helical structure, of collagen discovered by Ramachandran and Gopinath Kartha in 1954.

Ramachandran died on April 7, 2001.

Tribute to Ramachandran

In an editorial tribute in *Current Science* by P. Balaram and R. Ramasheshan, both of whom had seen Ramachandran in action and who are themselves accomplished scientists, wrote:

"Ramachandran was clearly a "Nobel Class" scientist, to borrow a phrase from Eugene Garfield. But his active career was all too brief by modem day standards. For the last twenty years Ramachandran was not really visible internationally, reminding us of one of the ironies of modern science; achievement alone is not enough, packaging and marketing play an important role. In India, where administrative positions are often considered a mark of scientific success Ramachandran was essentially an 'outsider' to the establishment. We have yet to learn that idiosyncratic

personalities often make the most original contribution to oil science. Ramachandran did all his work in India, following in the footsteps of his mentor, C.V. Raman.... Like man; extraordinary gifted individuals, Ramachandran often had an uneasy relationship with his surroundings. It was not easy for him to come to terms with mediocrity. Elevated to the formidable position of a head of the department at 30, he grew to be isolated from his colleagues, rarely establishing the easy academic relationships that make science a pleasure. But even at the height of his career Ramachandran most enjoyed scientific discussion; unfortunately his surroundings could rarely rise to the levels he demanded... In many ways, when the end came it was indeed time to go. But, Ramachandran has left behind a rich scientific legacy. His achievements will serve as a source of inspiration for generations to come. Ramachandran was undoubtedly one of the most outstanding scientists of post-independence India and truly, a jewel in the crown of India's science".

SUMMARY OF G.N. RAMACHANDRAN'S CAREER

Born on October 8,1922

Father : G.R. Narayana Iyer

Mother : Lakshmi Ammal

Education & Professional Occupation:

1939-42	BSc(Hons) Physics, St. Joseph's College, Trichy
1942-44	MSc Physics, India Institute, of Science (HSc), Bangalore
1944-47	DSc Physics, HSc (Under the supervision of Prof. C.V. Raman)
1947-49	PhD Crystallography, Cavendish laboratory, University of Cambridge, England

Professional Occupations:

1949-52	Assistant Professor of Physics, IISc Bangalore
1952-70	Professor & Head of Deptt. of Physics, University of Madras
1971-78	Professor & Head, Molecular Biophysics Unit, IISc, Bangalore
1978-81	Institute Professor, Mathematical Philosophy, IISc, Banglore
1981-84	CSIR Distinguished Scientist
1984-89	INSA Albert Einstein Professor, Mathematical Philosophy Group, IISc Bangalore

He also held the following assignments :
Director, Centre for Advanced Study in Biophysics &

Crystallography, University of Madras (1962-70); Jawaharlal Nehru Fellowship (1967-71); Part-time.

Membership in professional Scientific bodies.

Professor of Biophysics, University of Chicago, Chicago.

Fellow of the Indian National Science Academy

Fellow of the Royal Society of Arts, London

Fellow of the Royal Society, London

Founder Member of the Third World Academy of Sciences

Member, Council of International Union of Pure & applied Biophysics (1969-74)

Member, various Sub-commissions of the commission on Biochemical Nomenclature of the (1966-79).

Professor Ramachandran was a member of editorial boards of a number of national and international journals.

Membership in professional organisations/bodies (all are not included)

Important research Contributions:

His most important contributions were:

- Discovery of the triple helical structure of the connective tissue protein called collagen.
- 'The Ramachandran phi-psi Plot' which has become a standard description of protein structure.
- Development of the theory of image reconstruction from shadowgraphs (such as X-radiograms) using the Convolution Technique.
- Ramachandran received a number of national/ international awards.

Honors & Awards

1. Shanti Swarup Bhatnagar Prize for Physical Sciences (1961).

2. Watumul Memorial Prize in Biophysics (1964)
3. John Arthur Wilson Award by American Leather Chemist Association (1967).
4. Meghnad Saha Medal of the Asiatic Society (1971).
5. Srinivasa Ramanujan Medal of INSA (1972).
6. J.C. Bose Award of UGC (1976).
7. J.C. Bose Award of the Bose Institute (1977).
8. Fogarty International Medal of NIH (1978).
9. Indian Institute of Science Alumni Award (1979).
10. Sir C.V. Raman Medal of INSA (1982).
11. R.D. Birla Award for Medical Sciences (1985).
12. CSIR Golden Jubilee Award for Life Sciences (1991)
13. M.P. CSIR Jawaharlal Nehru Award for Sciences (1992).

He died on April 07, 2001

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